IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: |

S. C. Bauer et al. | GROUP ART UNIT: not assigned

5 SERIAL NUMBER: not assigned | EXAMINER: not assigned

FILED: February 26, 2002 | DATE: February 26, 2002

TITLE: Methods Of Ex-Vivo Expansion Of Hematopoietic Cells Using Multivariant (IL-3) Hematopoiesis Chimera Proteins

10   **PRELIMINARY AMENDMENT UNDER 37 C.F.R. § 1.111**

Assistant Commissioner of Patents
Washington, D. C. 20231

Sir:

15

Submitted herewith is a Preliminary Amendment under 37 C.F.R. § 1.111. Please

amend the application as follows:

20   IN THE SPECIFICATION

Please replace the first line of the specification with the following.

-- This is a divisional of United States Serial No. 08/762,227; which was filed
25 December 09, 1996, pending, which is a continuation-in-part of United States Serial
No. 08/446,872, filed June 06, 1995, which was filed under 35 U.S.C. § 371 from
PCT/US95/01185, filed February 04, 1995; which is a continuation-in-part of United
States Serial No. 08/192,325, filed February 04, 1994, now U.S. Patent No.
6,057,133: which a continuation-in-part of United States Serial No. 08/411,795, filed
30 April 06, 1995, now U.S. Patent No. 5,604,116, said 08/411,795 was filed under 35
U.S.C. § 371 fromPCT/US93/11197, filed November 22, 1993; which is continuation-
in-part of United States Serial No. 07/981,044 filed November 24, 1992, now
abandoned. The noted applications are incorporated herein by reference. --

35

                              IN THE CLAIMS

Please cancel claims 1-54 without prejudice.

Please add the following new claims 55-65.

-- 55. Cultured stem cells obtained from a method of ex vivo expansion of stem cells, comprising the steps of;

5   (a) culturing stem cells with a selected growth medium comprising a chimera protein having the formula selected from the group consisting of:

R_1-L-R_2, R_2-L-R_1, R_1-R_2, R_2-R_1, R_1-L-R_1 and R_1-R_1

10   wherein R_1 is a human interleukin-3 mutant polypeptide of SEQ ID NO:1

wherein

15   Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or Arg;

Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln;

Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;

Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;

Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu,

20   Gln, Asn, Thr, Ser or Val;

Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp,

          Asn, Gln, Leu, Val or Gly;

Xaa at position 23 is Ile, Val, Ala, Leu, Gly, Trp, Lys,

          Phe, Ser, or Arg;

25   Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu;

Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala;

Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp;

Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;

Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or Trp;

30   Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val;

Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, or

          Lys;

Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln;

Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or Glu;

35   Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu;

Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln,

Thr, Arg, Ala, Phe, Ile or Met;

Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val;

Xaa at position 36 is Asp, Leu, or Val;

5   Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile;

Xaa at position 38 is Asn, or Ala;

Xaa at position 40 is Leu, Trp, or Arg;

Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro;

Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr,

10   Leu, Val, Glu, Phe, Tyr, Ile, Met or Ala;

Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala,

Cys, Gln, Arg, Thr, Gly or Ser;

Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met,

Trp, Glu, Asn, Gln, Ala or Pro;

15   Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr,

Lys, Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His;

Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn,

Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;

Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His;

20   Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe,

Glu, Lys, Thr, Ala, Met, Val or Asn;

Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or Asp;

Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn,

Ser, Ala, Ile, Val, His, Phe, Met or Gln;

25   Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His;

Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr;

Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys,

Ser, or Met;

Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln,

30   Asn, Lys, His, Ala or Leu;

Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly;

Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg,

His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;

Xaa at position 57 is Asn or Gly;

35   Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;

Xaa at position 59 is Glu, Tyr, His, Leu, Pro, or Arg;

Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr;

Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;

Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile;

Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or Val;

5   Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys;

Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser;

Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;

Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, or

        His;

10   Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or His;

Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, or

        Leu;

Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;

Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr,

15   Gln, Trp, or Asn;

Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp;

Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg;

Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala;

Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg,

20   Ser, Gln, or Leu;

Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or

        Asp;

Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu;

Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;

25   Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or Asp;

Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or Arg;

Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or Lys;

Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn, His,

        Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;

30   Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met;

Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;

Xaa at position 85 is Leu, Asn, Val, or Gln;

Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;

Xaa at position 87 is Leu, Ser, Trp, or Gly;

35   Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;

Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn, or

Ser;

Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or Met;

Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or His;

Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala,

5   Gly, Ile or Leu;

Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or Arg;

Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln,

           Lys, His, Ala, or Pro;

Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly,

10   Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;

Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;

Xaa at position 97 is Ile, Val, Lys, Ala, or Asn;

Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr,

           Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;

15 Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln,

           Gly, Ser, Phe, or His;

Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln, or

           Pro;

Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,

20   Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln;

Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;

Xaa at position 103 is Asp, or Ser;

Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro,

           Leu, Gln, Lys, Ala, Phe, or Gly;

25 Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,

           Tyr, Leu, Lys, Ile, Asp, or His;

Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or Pro;

Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln,

           His, Ser, Ala or Pro;

30 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or Gly;

Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln,

           His, Glu, Ser, or Trp;

Xaa at position 111 is Leu, Ile, Arg, Asp, or Met;

Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or Phe;

35 Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr,

           Asp, Lys, Leu, Ile, Val or Asn;

5

Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu;

Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His,

     Thr, Trp, or Met;

Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val,

5

     Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or

     Ile;

Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro;

Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or Tyr;

Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or Arg;

10 Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln;

Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or Gly;

Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro,

     His, Ile, Tyr, or Cys;

Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu;

15

wherein from 1 to 14 amino acids can be deleted from the N-terminus and/or from 1 to 15 amino acids can be deleted from the C-terminus of said human interleukin-3 mutant polypeptide; and wherein from 4 to 44 of the amino acids

20 designated by Xaa are different from the corresponding amino acids of native (1-133) human interleukin-3;

R_2 is a hematopoietic growth factor;

25   L is a linker capable of Linking R_1 to R_2; and said chimera protein can additionally be immediately preceded by (methionine^{-1}), (alanine^{-1}), or (methionine^{-2}, alanine^{-1}); and

30   (b) harvesting said cultured stem cells.

    56. The cultured stem cells of claim 55 wherein said chimera protein is of the formula selected from the group consisting of:

35

R₁-L-R₂, R₂-L-R₁, R₁-R₂, R₂-R₁, R₁-L-R₁ and R₁-R₁

wherein R₁ is a human interleukin-3 mutant polypeptide of SEQ ID NO:4

5

wherein

Xaa at position 3 is Ser, Lys, Gly, Asp, Met, Gln, or Arg;

Xaa at position 4 is Asn, His, Leu, Ile, Phe, Arg, or Gln;

Xaa at position 5 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;

10 Xaa at position 6 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;

Xaa at position 7 is Asp, Phe, Lys, Arg, Ala, Gly, Glu,

    Gln, Asn, Thr, Ser or Val;

Xaa at position 8 is Glu, Trp, Pro, Ser, Ala, His, Asp,

    Asn, Gln, Leu, Val, or Gly;

15 Xaa at position 9 is Ile, Val, Ala, Gly, Trp, Lys,

    Phe, Ser, or Arg;

Xaa at position 10 is Ile, Gly, Val, Arg, Ser, Phe, or Leu;

Xaa at position 11 is Thr, His, Gly, Gln, Arg, Pro, or Ala;

Xaa at position 12 is His, Thr, Phe, Gly, Arg, Ala, or Trp;

20 Xaa at position 13 is Leu, Gly, Arg, Thr, Ser, or Ala;

Xaa at position 14 is Lys, Arg, Leu, Gln, Gly, Pro, Val or Trp;

Xaa at position 15 is Gln, Asn, Leu, Pro, Arg, or Val;

Xaa at position 16 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, or

    Lys;

25 Xaa at position 17 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln;

Xaa at position 18 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or Glu;

Xaa at position 19 is Pro, Leu, Gln, Ala, Thr, or Glu;

Xaa at position 20 is Leu, Val, Gly, Ser, Lys, Glu, Gln,

    Thr, Arg, Ala, Phe, Ile or Met;

30 Xaa at position 21 is Leu, Ala, Gly, Asn, Pro, Gln, or Val;

Xaa at position 22 is Asp, Leu, or Val;

Xaa at position 23 is Phe, Ser, Pro, Trp, or Ile;

Xaa at position 24 is Asn, or Ala;

Xaa at position 26 is Leu, Trp, or Arg;

35 Xaa at position 27 is Asn, Cys, Arg, Leu, His, Met, Pro;

Xaa at position 28 is Gly, Asp, Ser, Cys, Ala, Lys, Asn,

Thr, Leu, Val, Glu, Phe, Tyr, Ile or Met;

Xaa at position 29 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala,

Cys, Gln, Arg, Thr, Gly or Ser;

Xaa at position 30 is Asp, Ser, Leu, Arg, Lys, Thr, Met,

5   Trp, Glu, Asn, Gln, Ala or Pro;

Xaa at position 31 is Gln, Pro, Phe, Val, Met, Leu, Thr,

Lys, Asp, Asn, Arg, Ser, Ala, Ile, Glu, His or Trp;

Xaa at position 32 is Asp, Phe, Ser, Thr, Cys, Glu, Asn,

Gln, Lys, His, Ala, Tyr, Ile, Val or Gly;

10   Xaa at position 33 is Ile, Gly, Val, Ser, Arg, Pro, or His;

Xaa at position 34 is Leu, Ser, Cys, Arg, Ile, His, Phe,

Glu, Lys, Thr, Ala, Met, Val or Asn;

Xaa at position 35 is Met, Arg, Ala, Gly, Pro, Asn, His, or Asp;

Xaa at position 36 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn,

15   Ser, Ala, Ile, Val, His, Phe, Met or Gln;

Xaa at position 37 is Asn, Arg, Met, Pro, Ser, Thr, or His;

Xaa at position 38 is Asn, His, Arg, Leu, Gly, Ser, or Thr;

Xaa at position 39 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, or

Met;

20   Xaa at position 40 is Arg, Asp, Ile, Ser, Val, Thr, Gln,

Asn, Lys, His, Ala or Leu;

Xaa at position 41 is Arg, Thr, Val, Ser, Leu, or Gly;

Xaa at position 42 is Pro, Gly, Cys, Ser, Gln, Glu, Arg,

His, Thr, Ala, Tyr, Phe, Leu, Val or Lys;

25   Xaa at position 43 is Asn or Gly;

Xaa at position 44 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;

Xaa at position 45 is Glu, Tyr, His, Leu, Pro, or Arg;

Xaa at position 46 is Ala, Ser, Pro, Tyr, Asn, or Thr;

Xaa at position 47 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;

30   Xaa at position 48 is Asn, His, Val, Arg, Pro, Thr, Asp, or Ile;

Xaa at position 49 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or Val;

Xaa at position 50 is Ala, Asn, Pro, Ser, or Lys;

Xaa at position 51 is Val, Thr, Pro, His, Leu, Phe, or Ser;

Xaa at position 52 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;

35   Xaa at position 53 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, or

His;

8

Xaa at position 54 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or His;

Xaa at position 55 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, or Leu;

Xaa at position 56 is Asn, Leu, Val, Trp, Pro, or Ala;

Xaa at position 57 is Ala, Met, Leu, Pro, Arg, Glu, Thr,

Gln, Trp, or Asn;

Xaa at position 58 is Ser, Glu, Met, Ala, His, Asn, Arg, or Asp;

Xaa at position 59 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or Arg;

Xaa at position 60 is Ile, Met, Thr, Pro, Arg, Gly, Ala;

Xaa at position 61 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, Gln,

or, Leu;

Xaa at position 62 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, or

Asp;

Xaa at position 63 is Ile, Ser, Arg, Thr, or Leu;

Xaa at position 64 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;

Xaa at position 65 is Lys, Thr, Gly, Asn, Met, Arg, Ile, or Asp;

Xaa at position 66 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or Arg;

Xaa at position 67 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or Lys;

Xaa at position 68 is Leu, Gln, Lys, Trp, Arg, Asp, Glu,

Asn, His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;

Xaa at position 69 is Pro, Ala, Thr, Trp, Arg, or Met;

Xaa at position 70 is Cys, Glu, Gly, Arg, Met, or Val;

Xaa at position 71 is Leu, Asn, Val, or Gln;

Xaa at position 72 is Pro, Cys, Arg, Ala, or Lys;

Xaa at position 73 is Leu, Ser, Trp, or Gly;

Xaa at position 74 is Ala, Lys, Arg, Val, or Trp;

Xaa at position 75 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn, or

Ser;

Xaa at position 76 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or Met;

Xaa at position 77 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or His;

Xaa at position 78 is Pro, Phe, Arg, Ser, Lys, His, Ala,

Gly, Ile or Leu;

Xaa at position 79 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or Arg;

Xaa at position 80 is Arg, Ile, Ser, Glu, Leu, Val, Gln,

Lys, His, Ala or Pro;

Xaa at position 81 is His, Gln, Pro, Arg, Val, Leu, Gly,

Thr, Asn, Lys, Ser, Ala, Trp, Phe, Ile or Tyr;

9

Xaa at position 82 is Pro, Lys, Tyr, Gly, Ile, or Thr;

Xaa at position 83 is Ile, Val, Lys, Ala, or Asn;

Xaa at position 84 is His, Ile, Asn, Leu, Asp, Ala, Thr,

Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;

5 Xaa at position 85 is Ile, Leu, Arg, Asp, Val, Pro, Gln,

Gly, Ser, Phe, or His;

Xaa at position 86 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln, Pro;

Xaa at position 87 is Asp, Pro, Met, Lys, His, Thr, Val,

Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu or Gln;

10 Xaa at position 88 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;

Xaa at position 89 is Asp, or Ser;

Xaa at position 90 is Trp, Val, Cys, Tyr, Thr, Met, Pro,

Leu, Gln, Lys, Ala, Phe, or Gly;

Xaa at position 91 is Asn, Pro, Ala, Phe, Ser, Trp, Gln,

15 Tyr, Leu, Lys, Ile, Asp, or His;

Xaa at position 92 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or Pro;

Xaa at position 94 is Arg, Lys, Asp, Leu, Thr, Ile, Gln,

His, Ser, Ala, or Pro;

Xaa at position 95 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or Gly;

20 Xaa at position 96 is Lys, Asn, Thr, Leu, Gln, Arg,

His, Glu, Ser, Ala or Trp;

Xaa at position 97 is Leu, Ile, Arg, Asp, or Met;

Xaa at position 98 is Thr, Val, Gln, Tyr, Glu, His, Ser, or Phe;

Xaa at position 99 is Phe, Ser, Cys, His, Gly, Trp, Tyr,

25 Asp, Lys, Leu, Ile, Val or Asn;

Xaa at position 100 is Tyr, Cys, His, Ser, Trp, Arg, or Leu;

Xaa at position 101 is Leu, Asn, Val, Pro, Arg, Ala, His,

Thr, Trp, or Met;

Xaa at position 102 is Lys, Leu, Pro, Thr, Met, Asp, Val,

30 Glu, Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or

Ile;

Xaa at position 103 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro;

Xaa at position 104 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or Tyr;

Xaa at position 105 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or Arg;

35 Xaa at position 106 is Asn, Ala, Pro, Leu, His, Val, or Gln;

Xaa at position 107 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or Gly;

10

Xaa at position 108 is Gln, Ser, Met, Trp, Arg, Phe, Pro,

   His, Ile, Tyr, or Cys;

Xaa at position 109 is Ala, Met, Glu, His, Ser, Pro, Tyr, or Leu;

5   wherein from 4 to 44 of the amino acids designated by Xaa are different from the corresponding native amino acids of (1-133) human interleukin-3;

   R_2 is a hematopoietic growth factor;

10

   L is a linker capable of Linking R_1 to R_2; and said chimera protein can additionally be immediately preceded by (methionine^{-1}), (alanine^{-1}), or (methionine^{-2}, alanine^{-1}).

15   57. Cultured stem cells obtained from a method of ex vivo expansion of stem cells, comprising the steps of;

   (a) culturing stem cells with a selected growth medium comprising a chimera protein having the formula selected from
20   the group consisting of:

   R_1-L-R_2, R_2-L-R_1, R_1-R_2, R_2-R_1, R_1-L-R_1 and R_1-R_1

   wherein R_1 is a human interleukin-3 mutant polypeptide
25   of SEQ ID NO:7

wherein m is 0 or 1; Xaa at position 18 is Asn or Ile; Xaa at position 19 is Met, Ala or Ile; Xaa at position 20 is Ile, Pro or Leu; Xaa at position 23 is Ile, Ala or Leu; Xaa at
30   position 25 is Thr or His; Xaa at position 29 is Gln, Arg, Val or Leu; Xaa at position 32 is Leu, Ala, Asn or Arg; Xaa at position 34 is Leu or Ser; Xaa at position 37 is Phe, Pro, or Ser; Xaa at position 38 is Asn or Ala; Xaa at position 42 is Gly, Ala, Ser, Asp or Asn; Xaa at position 45 is Gln, Val,
35   or Met; Xaa at position 46 is Asp or Ser; Xaa at position 49

11

is Met, Ile, Leu or Asp; Xaa at position 50 is Glu or Asp; Xaa at position 51 is Asn Arg or Ser; Xaa at position 55 is Arg, Leu, or Thr; Xaa at position 56 is Pro or Ser; Xaa at position 59 is Glu or Leu; Xaa at position 60 is Ala or Ser; Xaa at position 62 is Asn, Val or Pro; Xaa at position 63 is Arg or His; Xaa at position 65 is Val or Ser; Xaa at position 67 is Ser, Asn, His or Gly; Xaa at position 69 is Gln or Glu; Xaa at position 73 is Ala or Gly; Xaa at position 76 is Ser, Ala or Pro; Xaa at position 79 is Lys, Arg or Ser; Xaa at position 82 is Leu, Glu, Val or Trp; Xaa at position 85 is Leu or Val; Xaa at position 87 is Leu, Ser, Trp; Xaa at position 88 is Ala or Trp; Xaa at position 91 is Ala or Pro; Xaa at position 93 is Pro or Ser; Xaa at position 95 is His or Thr; Xaa at position 98 is His, Ile, or Thr; Xaa at position 100 is Lys or Arg; Xaa at position 101 is Asp, Ala or Met; Xaa at position 105 is Asn or Gln; Xaa at position 109 is Arg, Glu or Leu; Xaa at position 112 is Thr or Gln; Xaa at position 116 is Lys, Val, Trp or Ser; Xaa at position 117 is Thr or Ser; Xaa at position 120 is Asn, Gln, or His; Xaa at position 123 is Ala or Glu; with the proviso that from four to forty-four of the amino acids designated by Xaa are different from the corresponding amino acids of native human interleukin-3);

R$_2$ is a hematopoietic growth factor;

L is a linker capable of Linking R$_1$ to R$_2$; and said chimera protein can additionally be immediately preceded by (methionine^{-1}), (alanine^{-1}), or (methionine^{-2}, alanine^{-1}); and

(b) harvesting said cultured stem cells.

58. Cultured stem cells obtained by the method of ex vivo expansion of stem cells, comprising the steps of;

12

(a) culturing said stem cells with a selected growth medium comprising a chimera protein having the formula selected from the group consisting of:

R_1-L-R_2, R_2-L-R_1, R_1-R_2, R_2-R_1, R_1-L-R_1 and R_1-R_1

wherein R_1 is a human interleukin-3 mutant polypeptide of SEQ ID NO:8

wherein m is 0 or 1; n is 0 or 1; p is 0 or 1; Xaa at position 4 is Asn or Ile; Xaa at position 5 is Met, Ala or Ile: Xaa at position 6 is Ile, Pro or Leu; Xaa at position 9 is Ile, Ala or Leu; Xaa at position 11 is Thr or His; Xaa at position 15 is Gln, Arg, Val or Leu; Xaa at position 18 is Leu, Ala, Asn or Arg; Xaa at position 20 is Leu or Ser; Xaa at position 23 is Phe, Pro, or Ser; Xaa at position 24 is Asn or Ala; Xaa at position 28 is Gly, Ala, Ser, Asp or Asn; Xaa at position 31 is Gln, Val, or Met; Xaa at position 32 is Asp or Ser; Xaa at position 35 is Met, Ile, Leu or Asp; Xaa at position 36 is Glu or Asp; Xaa at position 37 is Asn, Arg or Ser; Xaa at position 41 is Arg, Leu, or Thr; Xaa at position 42 is Pro or Ser; Xaa at position 45 is Glu or Leu; Xaa at position 46 is Ala or Ser; Xaa at position 48 is Asn, Val or Pro; Xaa at position 49 is Arg or His; Xaa at position 51 is Val or Ser; Xaa at position 53 is Ser, Asn, His or Gly; Xaa at position 55 is Gln or Glu; Xaa at position 59 is Ala or Gly; Xaa at position 62 is Ser, Ala or Pro; Xaa at position 65 is Lys, Arg or Ser; Xaa at position 67 is Leu, Glu, or Val; Xaa at position 68 is Leu, Glu, Val or Trp; Xaa at position 71 is Leu or Val; Xaa at position 73 is Leu, Ser or Trp; Xaa at position 74 is Ala or Trp; Xaa at position 77 is Ala or Pro; Xaa at position 79 is Pro or Ser; Xaa at position 81 is His or Thr; Xaa at position 84 is His, Ile, or Thr; Xaa at position 86 is Lys or Arg; Xaa at position 87 is Asp, Ala or Met; Xaa at position 91 is Asn or Glu; Xaa at position 95

13

is Arg, Glu, Leu; Xaa at position 98 Thr or Gln; Xaa at position 102 is Lys, Val, Trp or Ser; Xaa at position 103 is Thr or Ser; Xaa at position 106 is Asn, Gln, or His; Xaa at position 109 is Ala or Glu; with the proviso that from four

5 to forty-four of the amino acids designated by Xaa are different from the corresponding amino acids of native (15-125)human interleukin-3;

R_2 is a hematopoietic growth factor;

10

L is a linker capable of Linking R_1 to R_2; and said chimera protein can additionally be immediately preceded by (methionine^{-1}), (alanine^{-1}), or (methionine^{-2}, alanine^{-1}); and

15

(b) harvesting said cultured stem cells.

59. The cultured stem cells of claim 55 wherein R_1 is selected from the group consisting of:

20

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp
Val Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu
Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile
25 Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr
Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp
Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu
Asn Ala Gln Ala Gln Gln SEQ ID NO:9;

30 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu
Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile
Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr
35 Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp

Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu
Asn Ala Gln Ala Gln Gln SEQ ID NO:10;

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Val
5   Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp
Met Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu
Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile
Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr
Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp
10   Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu
Asn Ala Gln Ala Gln Gln SEQ ID NO:11;

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
15   Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu
Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Ala Ile
Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr
Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp
Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu
20   Asn Ala Gln Ala Gln Gln SEQ ID NO:12;

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu
25   Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Ala Ile
Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr
Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp
Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu
Asn Ala Gln Ala Gln Gln SEQ ID NO:13;
30

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
Gln Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu
Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Ala Ile
35   Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr
Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp

Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu
Asn Ala Gln Ala Gln Gln SEQ ID NO:14;

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
5   Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu
Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile
Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr
Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
10 Gln Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu
Asn Ala Gln Ala Gln Gln SEQ ID NO:15;

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
15 Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu
Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile
Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr
Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu
20 Asn Ala Gln Ala Gln Gln SEQ ID NO:16;

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu
25 Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile
Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr
Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp
Asn Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln Gln SEQ ID NO:17;
30

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu
Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile
35 Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr
Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp

16

Asn Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu
His Ala Gln Glu Gln Gln SEQ ID NO:18;

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu
Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile
Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr
Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln Gln SEQ ID NO:19;

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu
Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile
Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr
Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
Gln Ala Gln Glu Gln Gln SEQ ID NO:20;

Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp
Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu
Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Gly Ile
Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser Ala Thr
Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly Asp Trp
Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser Leu Glu
His Ala Gln Glu Gln Gln SEQ ID NO:21;

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp
Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu
Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Ala Ile
Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr
Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp

17

Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu
Asn Ala Gln Ala Gln Gln SEQ ID NO:22;

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
5   Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp
Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu
Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Ala Ile
Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr
Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp
10   Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu
Asn Ala Gln Ala Gln Gln SEQ ID NO:23;

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Val
Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp
15   Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu
Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Ala Ile
Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr
Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp
Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu
20   Asn Ala Gln Ala Gln Gln SEQ ID NO:24;

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
25   Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:25;
30

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
35   Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly

Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:26;

Met Ala Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu
Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly
Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn
Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln SEQ ID NO:27;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln SEQ ID NO:28;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly
Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln SEQ ID NO:29;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu
Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly

Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr
Leu Glu Asn Ala Gln Ala Gln Gln SEQ ID NO:30;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:31;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:32;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:33;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly

Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:34;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:35;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln SEQ ID NO:36;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln SEQ ID NO:37;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser
Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly

5

10

15

20

25

30

35

Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:38;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Val Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Thr Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Ser
Leu Glu His Ala Gln Glu Gln Gln SEQ ID NO:39;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Ser Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:40;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ala Ile His His Leu
Lys Arg Pro Pro Ala Pro Ser Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:41;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly

Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:42;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala
Glu Asp Val Asp Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:43;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:44;

Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu
Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp
Glu Asp Met Ser Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn
Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:45;

Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn
Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro
Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val
Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser
Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu
Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala

Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln
Ala Gln Glu Gln Gln SEQ ID NO:46;

5   Met Ala Tyr Pro Glu Thr Asp Tyr Lys Asp Asp Asp Asp Lys Asn
Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro
Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met
Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala
Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu
10   Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala
Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln
Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln
Ala Gln Glu Gln Gln SEQ ID NO:47; and

15   Met Ala Asn Cys Ser Ile Met Ile Asp Glu Leu Ile His His Leu
Lys Ile Pro Pro Asn Pro Ser Leu Asp Ser Ala Asn Leu Asn Ser
Glu Asp Val Ser Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn
Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser
Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser
20   Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly
Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr
Leu Glu Gln Ala Gln Glu Gln Gln SEQ ID NO:48.

     60. The cultured stem cells of claim 55, 56, 57, 58 or
25   59 wherein is R_2 is R_1 or a hematopoietic growth factor
selected from the group consisting of: GM-CSF, CSF-1, G-CSF,
G-CSF Ser[17], c-mpl ligand (MGDF or TPO), M-CSF,
erythropoietin (EPO), IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-
7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, IL-16, LIF,
30   flt3 ligand, human growth hormone, B-cell growth factor, B-
cell differentiation factor, eosinophil differentiation
factor, and stem cell factor (SCF);

     61. The cultured stem cells of claim 60 wherein is R_2
35   is selected from the group consisting of G-CSF, G-CSF Ser[17],
flt3 ligand, and c-mpl ligand.

24

62. The cultured stem cells of claim 56 wherein said chimera protein is selected from group consisting of: SEQ ID NO:121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131,
5   132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 165, 166, 167, and 168.

63. The cultured stem cells of claim 55, 56, 57, 58, 59,
10 or 62 wherein said culture medium further comprises a hematopoietic growth factor selected from the group consisting of: GM-CSF, CSF-1, G-CSF, G-CSF Ser^{17}, c-mpl ligand (MGDF or TPO), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12,
15 IL-13, IL-15, IL-16, LIF, flt3 ligand, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor (SCF).

64. The cultured stem cells of claim 60 wherein said
20 culture medium further comprises a hematopoietic growth factor selected from the group consisting of: GM-CSF, CSF-1, G-CSF, G-CSF Ser^{17}, c-mpl ligand (MGDF or TPO), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, IL-16, LIF, flt3
25 ligand, human growth hormone, B-cell growth factor, B-cell differentiation factor, eosinophil differentiation factor and stem cell factor (SCF).

65. The cultured stem cells of claim 62} wherein
30 said culture medium further comprises a hematopoietic growth factor selected from the group consisting of: GM-CSF, CSF-1, G-CSF, G-CSF Ser^{17}, c-mpl ligand (MGDF or TPO), M-CSF, erythropoietin (EPO), IL-1, IL-4, IL-2, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13,
35 IL-15, IL-16, LIF, flt3 ligand, human growth hormone, B-

cell growth factor, B-cell differentiation factor,
eosinophil differentiation factor and stem cell factor
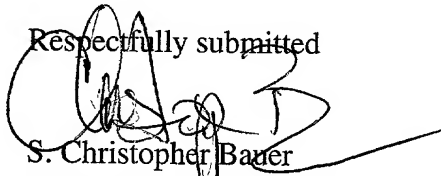(SCF). - -

5

REMARKS

Support for new claims 55-65 is found in claims 13-15 as filed, which were
subject to restriction in the parent application 08/762,227 (Paper No.9 dated
06/22/98), and in the claims from which they depended. New claims 55-65 are the
10   subject matter of claims 13-15 recast to include the limitations of the claims, from
which they depended.

Claims 1-54 have been canceled without prejudice. New claims 55-65 are
pending. No new matter has been added.

15

Respectfully submitted

S. Christopher Bauer
Registration No. 42,305
Tel: 636-737-6257

20

Pharmacia Corporation
Corporate Patent Department
800 N. Lindbergh Blvd.
Mail Zone O4E
25   St. Louis, MO 63167